REMARKS

Applicants respectfully request reconsideration and reexamination of the present application in light of the amendments and the remarks below.

Claims 1-24 are pending in this application. Claims 13-15 have been amended. These claim amendments are made to clarify the subject matter therein. Therefore, these amendments are submitted in order to place the claims in condition for allowance, and do not disclaim any subject matter to which the Applicants are entitled.

Rejection Under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 13 and 14 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention (Paper No. 11, page 3). Applicants respectfully traverse this rejection.

The Examiner stated that in claims 13 and 14, the term "characterized" is indefinite. The claims have been amended as suggested by the Examiner.

It is thus submitted that the claims 13 and 14 meet the requirements of 35 USC § 112, second paragraph, and reconsideration and withdrawal of the present rejection is respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-4 and 12 under U.S.C. § 103(a) as unpatentable over Himmler et al., (WO 97/31001; Reference N) (Paper No. 11, pages 2-3). Applicants respectfully traverse.

The Examiner stated that the "difference between the prior art compound and the instantly claimed compounds is the extent of the salt formation" (Paper No. 11, page 2). The present invention relates to semihydrochloride compounds. Himmler at al., discloses monohydrochloride compounds. As one skilled in the art would appreciate, it is generally quite unpredictable which kind of salts a given compound may form. Thus, the fact that a monohydrochloride of CCDC can be made, does by no means indicate that a semihydrochloride can be made as well. Furthermore, it is important to note that the semihydrochloride is not a mixture of a monohydrochloride and a free base, but a well-defined compound with distinct characteristics such as melting point and x-ray diffraction pattern.

The Examiner also stated that there are several nitrogen atoms present in the instant compound and it is possible to form 1 to 3 acid addition salts. Although the presence of nitrogens may lead the skilled person to prepare a dihydrochloride or trihydrochloride, there is no suggestion in the disclosure of Himmler et al., that would motivate one skilled in the art to prepare a semihydrochloride. Since there are three basic nitrogens available in the molecule, it would appear that preparing a semihydrochloride would, in fact, be unobvious. Furthermore, the prior art reference does not provide the requisite reasonable

expectation of success. That is, based on the disclosure of Himmler et al., it is not apparent that semihydrochloride compounds could actually be made, and that such a compound would be a stable, well-defined, distinct chemical entity. Thus, Himmler et al., does not teach or suggest all the claim limitations.

In addition, the Examiner stated that the "compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds" (Paper No. 11, page 3). As discussed in the previous reply (mailed October 9, 2002), a CCDC of formula (I) exhibited a solubility of 0.02% (w/w) (page 2), whereas a CCDC hydrochloride of formula (IV) demonstrated a solubility of 2.8% (w/w) (page 4). Surprisingly, the CCDC semihydrochloride exhibited a solubility of 19% (w/w) (page 5); considerably more soluble than the reference compound and the hydrochloride. Thus, unexpected results for the claimed compounds over those of the generic prior art compounds have been demonstrated.

It is therefore respectfully submitted that Himmler et al., (WO 97/31001) fail to teach or suggest the compounds as presently claimed, and that the current invention is novel and nonobvious in view of the prior art references. For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the present rejection.

CONCLUSION

For the foregoing reasons, Applicants submit that the claims are in condition for allowance and Applicants respectfully request reexamination of the present application, reconsideration and withdrawal of the present rejections, and entry of the amendments. Should there be any further matter requiring consideration, Examiner Robinson is invited to contact the undersigned counsel.

If there are any further fees due in connection with the filing of the present reply, please charge the fees to undersigned's Deposit Account No. 13-3372. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should also be charged to undersigned's deposit account.

Respectfully submitted,

Susan M. Pellegrino

April 14, 2003

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West Haven, CT 06516-4175
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Facsimile: (203) 812-6459

Claims (Attorney Docket No. Mo 6341/LeA 33 270)

1. (Original) Semi-hydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid.

2. (Previously amended) Semi-hydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo-[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid (CCDC semihydrochloride), having an X-ray powder diffractogram with the following reflection signals (2 theta) of high and medium intensity.

θ (2 Theta)
5.86
6.90
7.26
8.98
9.35
10.13
10.68
10.97
12.41
13.67
14.57
14.89
15.73
16.07
16.47
16.87
17.78
18.91
19.81
20.04
20.62
20.75
20.93
21.46
21.74
22.92
25.36
25.71
26.98
27.58
28.24
30.61

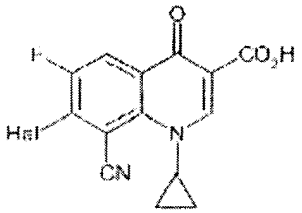
3. (Previously amended) Semi-hydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo-[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid (CCDC semihydrochloride), having X-ray powder diffractogram with the following reflection signals (2 theta) of high and medium intensity.

2 θ (2 Theta)
5.86
6.90
7.26
8.98
9.35
10.13
10.68
10.97
12.41
13.67
14.57
14.89
15.73
16.07
16.47
16.87
17.78
18.91
19.81
20.04
20.62
20.75
20.93
21.46
21.74
22.92
25.36

25.71
26.98
27.58
28.24
30.61

and a melting point, determined by DTA, of from 278°C to 280°C.

4. (Previously amended) CCDC semihydrochloride according to Claim 1, obtainable by reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline-carboxylic acid of the formula (II)

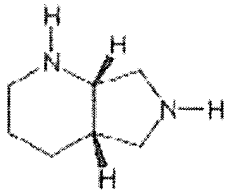


(II),

in which

Hal represents fluorine or chlorine,

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III),

optionally in the presence of a base, in one of the following diluents or diluent mixtures:

a) aliphatic alcohols selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol,

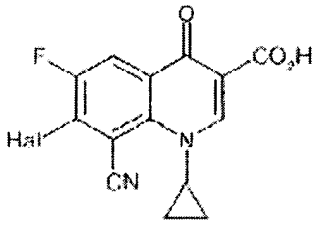
b) mixture of aliphatic alcohols selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

5. (Previously amended) A process for preparing CCDC semihydrochloride according to Claim 1, comprising reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

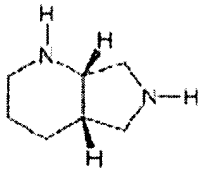


(II),

in which

Hal represents fluorine or represents chlorine

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols selected from the group consisting of butanol, isobutanol, 2-butanol,

tert-butanol, and 1-pentanol,

b) mixture of aliphatic alcohols selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

6. (Previously amended) A process for preparing CCDC semihydrochloride according to Claim 5, wherein the diluent used is an aliphatic alcohol selected from the group consisting of butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol or that an aliphatic alcohol selected from the group consisting of ethanol, propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol is used as component of a diluent mixture.

7. (Previously amended) A process for preparing CCDC semihydrochloride according to Claim 5, wherein if an aliphatic alcohol selected from the group consisting of propanol, isopropanol, butanol, isobutanol, 2-butanol, tert-butanol, and 1-pentanol is used as component of a diluent mixture, N-methyl-pyrrolidone is simultaneously employed as a further diluent in a ratio of from 1 to 1 to 3 to 1.

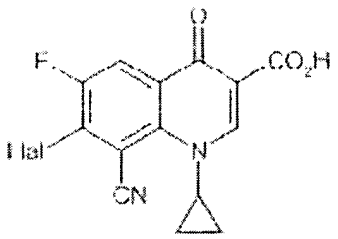
8. (Previously amended) Process for preparing CCDC semihydrochloride according to Claim 6, wherein if propanol is used as component of a diluent mixture, N,N-dimethylformamide is simultaneously employed as further diluent in a ratio of from 1 to 1 to 3 to 1.

9. (Previously amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 1.

10. (Previously amended) A method of preparing a pharmaceutical composition comprising formulating CCDC semihydrochloride according to Claim 1.

11. (Previously amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 1.

12. (Original) CCDC semihydrochloride according to Claim 2, obtainable by reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline-carboxylic acid of the formula (II)

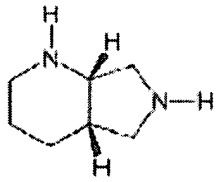


(II),

in which

Hal represents fluorine or chlorine,

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

optionally in the presence of a base, in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbons,

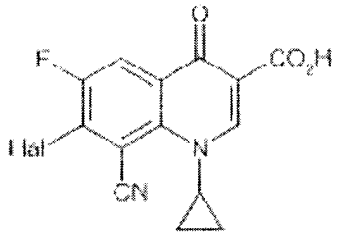
b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorphine and/or N-butylmorphine base.

13. (Currently amended) A process for preparing a CCDC semihydrochloride as defined in Claim 2, ~~characterized in that~~ wherein 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

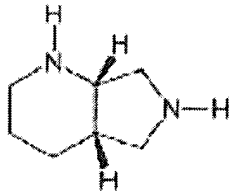


(II),

in which

Hal represents fluorine or represents chlorine

and (1S, 6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

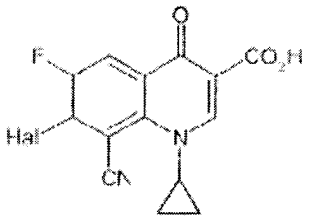
b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

14. (Currently amended) A process for preparing a CCDC semihydrochloride as defined in Claim 3, ~~characterized in that~~ wherein 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

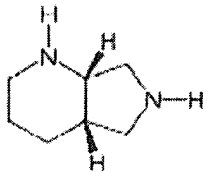


(II),

in which

Hal represents fluorine or represents chlorine

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

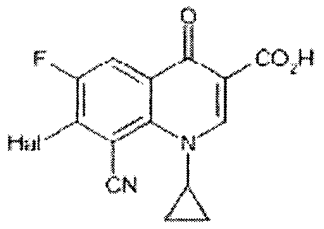
b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

15. (Currently amended) A process for preparing a CCDC semihydrochloride as defined in Claim 4, ~~characterized in that~~ wherein 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

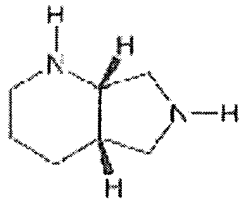


(II),

in which

Hal represents fluorine or represents chlorine

and (1 S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

a) aliphatic alcohols having at least four carbon atoms,

b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,

c) mixture of propanol and N,N-dimethylformamide,

or

d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

16. (Previously amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 2.

17. (Previously amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 3.

18. (Previously amended) A pharmaceutical composition comprising, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 4.

19. (Previously amended) A method of preparing a pharmaceutical composition comprising formulating CCDC semihydrochloride as defined in Claim 2.

20. (Previously amended) A method of preparing a pharmaceutical composition comprising formulating CCDC semihydrochloride as defined in Claim 2.

21. (Previously amended) A method of preparing pharmaceutical composition comprising formulating CCDC semihydrochloride as defined in Claim 1.

22. (Previously amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 2.

23. (Previously amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 3.

24. (Previously amended) A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride as defined in Claim 4.